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| EXAMINER | |
|---|---|
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/534,990 | HEIM ET AL. | |
| | Examiner | Art Unit | |
| | Molly E. Baughman | 1637 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *29-38* is/are pending in the application.

4a) Of the above claim(s) *30-36 and 38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29 and 37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 November 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Election/Restrictions*

1. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 29 and 37, drawn to a labeled or unlabelled nucleic acid comprising SEQ ID NO:1, 2, and/or 3, or those with homology greater than 78%, or complements thereof, and kits thereof.

Group II, claim(s) 30-36, and 38, drawn to a method for detection of Human Adenovirus DNA in a sample.

2. The inventions listed as Groups I-II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the special technical feature of claim 1, a labeled or unlabelled nucleic acid comprising SEQ ID NO:1, or 3, or those with homology greater than 78%, or complements thereof, does not provide contribution over the prior art (see Roy et al. (WO/98/32842, Figure 1B, Adenovirus 12 sequence, which comprises the complement of SEQ ID NO:1, and a sequence having 89% homology to SEQ ID NO:3).

3. During a telephone conversation with Amy Dobbelaere on 9/5/08 a provisional election was made with traverse to prosecute the invention of Group I, claims 29 and 37. Affirmation of this election must be made by applicant in replying to this Office action. Applicants argued that searching the methods would not be an undue burden with the search of Group I because they are both directed to the same sequences. This is not found persuasive because a method comprising various steps of (1) providing a

probe that can specifically bind to the DNA of at least 35 different HAdV serotypes, and (2) amplifying regions of DNA of each of said at least 35 HAdV serotypes actually present in the sample, includes a search for various sequences which can bind to at least 35 different HAdV serotypes, and not necessarily just those included in claim 29 or 37. Furthermore, the sequences of SEQ ID NO: 1, 2, and 3 could be used in various methods such as array hybridization, ligation chain reaction, linker mediated amplification reaction, etc.

4. Claims 30-36 and 38 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

5. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

6. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

***Claim Rejections - 35 USC § 112***

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 29 and 37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 29 and 37 use open language and encompass sequences of an unlimited size, larger than the claimed SEQ ID NO:1, 2, and 3, as well as sequences encompassing those having at least 78% homology to such sequences, presenting a large number of sequences and sequence variations, which are not supported in the specification. For example, claim 29 is drawn to sequences comprising a sequence with homology greater than 78% with respect to SEQ ID NO:1, where this encompasses sequences which comprise unlimited 5' and 3' flanking sequences. Such sequences are not adequately described in the specification.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 29 and 37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 29 and 37 are confusing because it is unclear what is encompassed by "complementary." It is unclear if "complementary" is intended to include mismatches or if it means "fully complementary." If the latter, it is suggested to amend such language into the claim.

***Claim Rejections - 35 USC § 101***

11. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

12. Claim 29 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claim 29 and 37 encompasses sequences which constitute a product of nature. MPEP 706.03(a) states that "the subject matter of the invention or discovery must come within the boundaries set forth by 35 U.S.C. 101, which permits patents to be granted only for "any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof...a thing occurring in nature, which is substantially unaltered, is not a "manufacture." A shrimp with the head and digestive tract removed is an example. *Ex parte Grayson*, 51 USPQ 413 (Bd. App. 1941)." Claim 29 is broadly drawn to an unlabelled nucleic acid comprising the sequence SEQ ID NO:1 or SEQ ID NO:3, or a sequence with homology greater than 78% with respect to SEQ ID NO:1 or SEQ ID NO:3, or complements thereof, which includes sequences of an unlimited size, which are not isolated, and therefore, encompasses those naturally occurring in nature and is non-statutory subject matter.

***Claim Rejections - 35 USC § 102***

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. Claim 29 is rejected under 35 U.S.C. 102(b) as being anticipated by Roy et al. (WO/98/32842 A1, published 6/30/08).

Roy et al. teach a sequence in Figure 1B, labeled Human adenovirus 12 hexon nucleotide sequence, which comprises the complement of SEQ ID NO:1 (i.e. part (a) and (c)), and a sequence with 89% homology to SEQ ID NO:3 (i.e. part b).

15. Claim 29 is rejected under 35 U.S.C. 102(b) as being anticipated by Seed et al. (WO/2002/020814, published 3/14/02).

Seed et al. teach the sequence of SEQ ID NO:4 (pg.21 of sequence listing in specification), which comprises a sequence with 93% homology to SEQ ID NO:1 (i.e. part (b)).

16. Claim 29 is rejected under 35 U.S.C. 102(e) as being anticipated by Wilson et al. (WO/2003/046124 A2, priority date 11/21/01).

Wilson et al. teach the sequence of SEQ ID NO:34 (see claim 1, and pg.184 of the sequence listing), which comprises the complement of SEQ ID NO:3 (i.e part (a) and (c)).

***Claim Rejections - 35 USC § 103***

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

18. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

19. Claim 37 is rejected under 35 U.S.C. 103(a) as being unpatentable over Vivaud et al. (US 6,541,246) in view of Roy et al. (WO/98/32842 A1), and further in view of Buck et al., "Design Strategies and Performance of Custom DNA Sequencing Primers," Biotechniques, Sept. 1999, Vol.27, No.3, pp. 528-536.

Vivaud et al. teach a kit comprising two primers and a probe for detecting Human Adenoviruses (see col.4, lines 54-63).

Vivaud et al. do not teach the sequences of SEQ ID NO:1, 2, or 3, or sequences having at least 78% homology thereof.

Roy et al. teach a sequence in Figure 1B, labeled Human adenovirus 12 hexon nucleotide sequence, which comprises the complement of SEQ ID NO:1 (i.e. part (a) and (c)), a sequence with 89% homology to SEQ ID NO:3 (i.e. part e), and the sequence of SEQ ID NO:2 (i.e. part a).

In the court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the Court of Appeals for the Federal Circuit determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologs, however, the Court stated,

"Normally, a *prima facie* case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties."

Since the claimed primers simply represent structural homologs, which are derived from sequences of Human Adenoviruses known in the art and concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed primers are *prima facie* obvious over the cited references in the absence of secondary considerations.

Buck expressly provides evidence of the equivalence of primers. Specifically, Buck invited primer submissions from a number of labs (39) (page 532, column 3), with 69 different primers being submitted (see page 530, column 1). Buck also tested 95 primers spaced at 3 nucleotide intervals along the entire sequence at issue, thereby testing more than 1/3 of all possible 18 mer primers on the 300 base pair sequence (see page 530, column 1). When Buck tested each of the primers selected by the methods of the different labs, Buck found that EVERY SINGLE PRIMER worked (see page 533, column 1). Only one primer ever failed, No. 8, and that primer functioned when repeated. Further, EVERY SINGLE CONTROL PRIMER functioned as well (see page 533, column 1). Buck expressly states "The results of the empirical sequencing analysis were surprising in that nearly all of the primers yielded data of extremely high quality (page 535, column 2)." Therefore, Buck provides direct evidence that all primers would be expected to function, and in particular, all primers selected according to the ordinary criteria, however different, used by 39 different laboratories. It is particularly striking that all 95 control primers functioned, which represent 1/3 of all possible primers in the target region. This clearly shows that every primer would have a reasonable expectation of success.

One of ordinary skill in the art would have been motivated to build a kit and include the primers of SEQ ID NO: 1, 2, and probe of SEQ ID NO:3, or sequences having at least 78% homology thereof, because Vivaud et al. demonstrate that it was conventional in the art to build a kit and include primers and probes to amplify and detect adenoviruses, and Roy et al. show that the adenovirus sequence, comprising such sequences, was known in the art at the time of the invention. Furthermore, Buck et al. demonstrate the capability of multiple primers to equivalently amplify the same targeted region. Therefore, the skilled artisan would have had a reasonable expectation of success in making a kit, and including similar primers and probes to those of Vivaud et al., derived from the sequences of Roy et al. It would have been obvious to one of ordinary skill in the art at the time of the invention to build the claimed kit, and include the claimed primers comprising SEQ ID NO:1 and 2, and the probe of SEQ ID NO:3, or sequences having at least 78% homology, therein.

20. Claim 37 is rejected under 35 U.S.C. 103(a) as being unpatentable over Vivaud et al. (US 6,541,246) in view of Roy et al. (WO/98/32842 A1), in view of Wilson (WO/2003/046124 A2), and further in view of Buck et al., "Design Strategies and Performance of Custom DNA Sequencing Primers," Biotechniques, Sept. 1999, Vol.27, No.3, pp. 528-536.

Vivaud et al. teach a kit comprising two primers and a probe for detecting Human Adenoviruses (see col.4, lines 54-63).

Vivaud et al. do not teach the sequences of SEQ ID NO:1, 2, or 3, or sequences having at least 78% homology thereof.

Roy et al. teach a sequence in Figure 1B, labeled Human adenovirus 12 hexon nucleotide sequence, which comprises the complement of SEQ ID NO:1 (i.e. part (a) and (c)), a sequence with 89% homology to SEQ ID NO:3 (i.e. part e), and the sequence of SEQ ID NO:2 (i.e. part a).

Roy et al. do not teach such sequences comprising the exact sequence of SEQ ID NO:3.

Wilson et al. teach the sequence of SEQ ID NO:34 (see claim 1, and pg.184 of the sequence listing), which comprises the complement of SEQ ID NO:3 (i.e part (d) and (f)).

In the court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the Court of Appeals for the Federal Circuit determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologs, however, the Court stated,

"Normally, a *prima facie* case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties."

Since the claimed primers simply represent structural homologs, which are derived from sequences of Human Adenoviruses known in the art and concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with

improved properties, the claimed primers are *prima facie* obvious over the cited references in the absence of secondary considerations.

Buck expressly provides evidence of the equivalence of primers. Specifically, Buck invited primer submissions from a number of labs (39) (page 532, column 3), with 69 different primers being submitted (see page 530, column 1). Buck also tested 95 primers spaced at 3 nucleotide intervals along the entire sequence at issue, thereby testing more than 1/3 of all possible 18 mer primers on the 300 base pair sequence (see page 530, column 1). When Buck tested each of the primers selected by the methods of the different labs, Buck found that EVERY SINGLE PRIMER worked (see page 533, column 1). Only one primer ever failed, No. 8, and that primer functioned when repeated. Further, EVERY SINGLE CONTROL PRIMER functioned as well (see page 533, column 1). Buck expressly states "The results of the empirical sequencing analysis were surprising in that nearly all of the primers yielded data of extremely high quality (page 535, column 2)." Therefore, Buck provides direct evidence that all primers would be expected to function, and in particular, all primers selected according to the ordinary criteria, however different, used by 39 different laboratories. It is particularly striking that all 95 control primers functioned, which represent 1/3 of all possible primers in the target region. This clearly shows that every primer would have a reasonable expectation of success.

One of ordinary skill in the art would have been motivated to build a kit and include the primers of SEQ ID NO: 1, 2, and probe of SEQ ID NO:3 because Vivaud et al. demonstrate that it was conventional in the art to build a kit and include primers and probes to amplify and detect adenoviruses; Roy et al. show that the adenovirus sequence, comprising the sequences of SEQ ID NO:1 and 2, was known in the art at the time of the invention; and Wilson demonstrates that the adenovirus sequence, comprising the sequence of SEQ ID NO:3, was known in the art at the time of the invention. Furthermore, Buck et al. demonstrate the capability of multiple primers to equivalently amplify the same targeted region. Therefore, the skilled artisan would have had a reasonable expectation of success in making a kit, and including similar primers and probes to those of Vivaud et al., derived from the sequences of Roy et al. and

Wilson et al. It would have been obvious to one of ordinary skill in the art at the time of the invention to build the claimed kit, and include the claimed primers comprising SEQ ID NO:1 and 2, and the probe of SEQ ID NO:3, therein.

***Summary***

21. No claims are free of the prior art.

22. Hegele et al. (CA 2231271), teaching a primer having 93.6% homology to SEQ ID NO:2 (Database Accession Number AAX03293), is noted as a reference of interest.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Molly E. Baughman whose telephone number is (571)272-4434. The examiner can normally be reached on Monday-Friday 8-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kenneth R Horlick/
Primary Examiner, Art Unit 1637

/Molly E Baughman/
Examiner, Art Unit 1637